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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,029	CONN ET AL.	
	Examiner	Art Unit	
	LESLIE A. ROYDS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6,7,10-12 and 14-23* is/are pending in the application.

4a) Of the above claim(s) *6,7,11,12 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,14 and 19-23* is/are rejected.

7)☒ Claim(s) *3,10,14 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 6-7, 10-12 and 14-23 are presented for examination.

Applicant's Amendment filed April 15, 2009 has been received and entered into the present application. Applicant's specification at p.8 has been amended.

Claims 1, 3, 6-7, 10-12 and 14-23 are pending. Claims 6-7, 11-12 and 15-18 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b). Claims 19-23 are newly added. Claim 1 is amended. Claims 1, 3, 10, 14 and 19-23 are under examination.

Applicant's arguments, filed April 15, 2009, have been fully considered be persuasive. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Error Noted in Claim Listing Dated April 15, 2009

Applicant has indicated the status of instant claims 3 and 14 as "Withdrawn" in the claim listing filed with the amendment submission dated April 15, 2009. However, as noted in the non-final rejection dated February 3, 2009, instant claims 3 and 14 have been examined and are not properly withdrawn from consideration at this time. Accordingly, claims 3 and 14 are under examination, despite the incorrect status identifier provided in the claim listing of April 15, 2009, and are herein examined on the merits.

Objection to the Claims (New Grounds of Objection)

Claims 3 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. In the instant case, parent claim 1 is directed to the treatment of Parkinson's disease, which is again

recited in instant claims 3 and 14. Accordingly, it is unclear how instant claims 3 and 14 are intended to further limit the subject matter of instant claim 1. Correction is required.

Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 20 is objected to for failing to define the acronym "FLIPR" in the phrase "FLIPR assay" at its first occurrence in the claims.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement

(New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 14 and 19-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Present claim 1 is directed to a method of treatment of Parkinson's disease in a patient in need thereof that comprises administering to the patient a therapeutically effective amount of an mGluR4 receptor positive allosteric modulator or a pharmaceutically acceptable salt thereof.

Present claim 19 specifies that the mGluR4 receptor positive allosteric modulator possesses a selectivity for the mGluR4 receptor relative to each of the other mGluR receptors by at least three to 300 fold or greater as measured by the ratio of EC_{50}.

Present claim 20 specifies that the mGluR4 receptor positive allosteric modulator possesses an

EC_{50} for binding to the mGluR4 receptor of 1 μM to 1 nM or less as evaluated by the FLIPR assay.

Present claim 21 specifies that the mGluR4 receptor positive allosteric modulator is a non-peptidyl mGluR4 receptor positive allosteric modulator.

Present claim 22 specifies that the mGluR4 receptor positive allosteric modulator is a peptidyl mGluR4 receptor positive allosteric modulator.

Present claim 23 specifies that the mGluR4 receptor positive allosteric modulator is a compound that exhibits sufficient concentration in the central nervous system to have a therapeutic efficacy upon oral administration.

In particular, the specification as originally filed fails to provide adequate written description for (1) the claimed genus of mGluR4 receptor positive allosteric modulators (claim 1); (2) the claimed genus of mGluR4 receptor positive allosteric modulators that possess a selectivity for the mGluR4 receptor relative to each of the other mGluR receptors by at least three to 300 fold or greater as measured by the ratio of EC_{50} (claim 19); (3) the claimed genus of mGluR4 receptor positive allosteric modulators that possess an EC_{50} for binding to the mGluR4 receptor of 1 μM to 1 nM or less as evaluated by the FLIPR assay (claim 20); (4) the claimed genus of non-peptidyl mGluR4 receptor positive allosteric modulators (claim 21); (5) the claimed genus of peptidyl mGluR4 receptor positive allosteric modulators (claim 22); or (6) the claimed genus of mGluR4 receptor positive allosteric modulators that exhibit sufficient concentration in the central nervous system to have a therapeutic efficacy upon oral administration (claim 23).

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli*

Lilly, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for *Examination of Patent Applications* under the 35 U.S.C. 112.1 "Written Description" Requirement ("*Guidelines*"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure…" *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Applicant provides various functional descriptions of the possible mGluR4 receptor positive allosteric modulators at p.5-6 of the instant specification, but describes only a single compound (i.e., N-phenyl-7-(hydroxylimino)-cyclo-propa[b]-chromen-1a-carboxamide) as an mGluR4 receptor positive allosteric modulator (see, e.g., claim 10 and p.6 of the instant specification). Aside from this single compound, Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties, aside from these specific functional properties (i.e., (1) mGluR4 receptor positive allosteric modulators, (2) mGluR4 receptor positive allosteric modulators that possess a selectivity for the mGluR4 receptor relative to each of the other mGluR receptors by at least three to 300 fold or greater as measured by the ratio of EC_{50}; (3) mGluR4 receptor positive allosteric modulators that possess an EC_{50} for binding to the mGluR4 receptor of 1 μM to 1 nM or less as evaluated by the FLIPR assay; (4) non-peptidyl mGluR4 receptor positive allosteric modulators; (5) peptidyl mGluR4 receptor positive allosteric modulators; or (6) mGluR4 receptor positive allosteric modulators that exhibit sufficient concentration in the central nervous system to have a therapeutic efficacy upon oral administration), that would provide adequate written description of these claimed genera of compounds capable of performing such

function(s) that Applicant was actually in possession of, and intended to be used within the context of the present invention, at the time of the invention, aside from the single compound N-phenyl-7-(hydroxylimino)-cyclo-propa[b]-chromen-1a-carboxamide.

MPEP §2163 recites, "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the claimed genus." Please reference *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Applicant has failed to define any structural component, such as a common core structural element, as being responsible for the function of the compounds as being mGluR4 receptor positive allosteric modulators (or mGluR4 receptor positive allosteric modulators with the specific properties identified in instant claims 19-23), and, thus, has failed to define the metes and bounds of the claimed genera of compounds. While it is duly noted that the genus of mGluR4 receptor positive allosteric modulators (or those modulators with the specific properties identified in instant claims 19-23) is limited to those capable of functioning in this manner, it remains that Applicant has not appropriately defined the metes and bounds of the genus, even when limited by function. Adequate description of a compound used for a specific function (e.g., in this case, a compound that functions as an mGluR4 receptor positive allosteric modulator) may be provided if the written description adequately links or associated an adequately described *particular structure, material, or act to the function* or if it is clear *based on the facts of the application that one skilled in the art would have known what structure, material or acts would perform the function*. On its face, the instant application does not appear to meet either of these criteria. The specification provides no disclosure beyond the generic disclosure of the required function

that would correlate a common structural element or material to performance of the claimed function that would be readily identifiable to one of skill in the art. Further, Applicant has failed to establish on the record that the state of the art was sufficiently well-developed that one of ordinary skill in the art at the time of the invention would have immediately envisaged the types of compounds that would perform the claimed function(s) in the instant specification. In other words, the present specification provides no disclosure beyond the generic disclosure of the required functions that would provide a means for identifying the compounds that would have been amenable for use in the present invention (aside from the one specifically named compound N-phenyl-7-(hydroxylimino)-cyclo-propa[b]-chromen-1a-carboxamide), nor does it specifically teach a common structural element that performs the function recited in the claim and would be readily identifiable to one of skill in the art. Furthermore, it has been held that a wish or plan for obtaining the chemical invention as claimed does not provide adequate written description of a chemical invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof, is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.,* 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

While it is recognized that adequate written description of a limitation is not required to be stated *in haec verba* in the specification or claims as originally filed, adequate written support for claim limitations must arise from either an explicit or implicit suggestion by the disclosure to show that such a concept as claimed was actually in possession of Applicant at the time of the invention. For the reasons provided *supra*, Applicant has failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of (1) the claimed genus of mGluR4 receptor positive allosteric modulators (claim 1); (2) the claimed genus of mGluR4 receptor positive allosteric modulators that possess a selectivity for the mGluR4 receptor relative to each of the other mGluR receptors by at least three to 300 fold or greater as measured by the

ratio of EC_{50} (claim 19); (3) the claimed genus of mGluR4 receptor positive allosteric modulators that possess an EC_{50} for binding to the mGluR4 receptor of 1 μM to 1 nM or less as evaluated by the FLIPR assay (claim 20); (4) the claimed genus of non-peptidyl mGluR4 receptor positive allosteric modulators (claim 21); (5) the claimed genus of peptidyl mGluR4 receptor positive allosteric modulators (claim 22); or (6) the claimed genus of mGluR4 receptor positive allosteric modulators that exhibit sufficient concentration in the central nervous system to have a therapeutic efficacy upon oral administration (claim 23).

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 3 is directed to the method of claim 1, wherein the movement disorder is selected from the group consisting of Parkinson's disease, dyskinesia, etc.

Present claim 14 is directed to the method of claim 1, wherein the movement disorder is Parkinson's disease.

In particular, there is insufficient antecedent basis for the limitation “the movement disorder” in line 1 of each of claims 3 and 14, since the preceding text of the claims or those from which they depend fail to set forth any reference to “a movement disorder” *per se*.

Furthermore, instant claim 3 is also directed to a multitude of other various movement disorders,

whose relationship to the primary therapeutic objective of treating Parkinson's disease has not been clearly, precisely or deliberately set forth. As a result, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 19 is directed to the method of claim 1, wherein the mGluR4 receptor positive allosteric modulator possesses a selectivity for the mGluR4 receptor relative to each of the other mGluR receptors by at least three to 300 fold or greater as measured by the ratio of EC_{50}.

In particular, it is unclear what range of selectivity values are intended to be circumscribed by the instant claims. Specifically, instant claim 19 states that the modulator has a selectivity for the mGluR4 receptor relative to the other mGluR receptors of at least 3 to 300 fold or greater, but the claim fails to clearly, precisely or deliberately set forth whether the selectivity ratio ranges from (1) 3 to 300 fold, (2) 3 fold or greater, or (3) 300 fold or greater. As a result of this ambiguity in the claim language, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection. Clarification is requested.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 20 is directed to the method of claim 1, wherein the mGluR4 receptor positive allosteric modulator possesses an EC_{50} for binding to the mGluR4 receptor of 1 μM to 1 nM or less as evaluated by the FLIPR assay.

In particular, it is unclear what range of EC_{50} values are intended to be circumscribed by the instant claims. Specifically, instant claim 20 states that the modulator has an EC_{50} of 1 μM to 1 nM or less, but the claim fails to clearly, precisely or deliberately set forth whether the EC_{50} ranges from (1) 1 μM to 1 nM, (2) 1 μM or less, or (3) 1 nM or less. As a result of this ambiguity in the claim language, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection. Clarification is requested.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

Conclusion

Rejection of claims 1, 3, 14 and 19-23 is proper.

Claim 10 is objected to for depending from a rejected base claim.

Claims 6-7, 11-12 and 15-18 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE A. ROYDS whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

June 29, 2009

/Ardin Marschel/
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